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Association of residential air pollution, noise, and greenspace with initial ischemic stroke severity.

Rosa Maria Vivanco-Hidalgo[a,*], Carla Avellaneda-Gómez[a,b], Payam Dadvand[c,d], Marta Cirach[c], Ángel Ois[a], Alejandra Gómez González[a], Ana Rodriguez-Campello[a], Pablo de Ceballos[a], Xavier Basagaña[c,d,e], Ana Zabalza[a], Elisa Cuadrado-Godia[a], Jordi Sunyer[c,d,e], Jaume Roquer[a,**], Gregory A. Wellenius[f]

[a] Hospital del Mar Medical Research Institute, C/DrAiguader 88, CP08003, Barcelona, Spain
[b] Universitat Autònoma de Barcelona (UAB), Barcelona, Spain
[c] BarcelonaInstitute for Global Health (ISGlobal), C/DrAiguader 88, CP08003, Barcelona, Spain
[d] Universitat PompeuFabra (UPF), Barcelona, Spain
[e] CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain
[f] Department of Epidemiology, Brown University School of Public Health, Providence, RI 02912, USA

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ABSTRACT

Background and Purpose: A number of environmental risk factors of acute ischemic stroke have been identified, but few studies have evaluated the influence of the outdoor environment on stroke severity. We assessed the association of residential ambient fine particulate matter air pollution ($PM_{2.5}$), noise, and surrounding greenspace with initial stroke severity.

Methods: We obtained data on patients hospitalized with acute ischemic stroke from a hospital-based prospective stroke register (2005–2014) in Barcelona. We estimated residential $PM_{2.5}$ based on an established land use regression model, greenspace as the average satellite-based Normalized Difference Vegetation Index (NDVI) within a 300 m buffer of the residence, and daily (*Lday*), evening (*Levening*), night (*Lnight*) and average noise (*Lden*) level at the street nearest to the residential address using municipal noise models. Stroke severity was assessed at the time of hospital presentation using the National Institute of Health Stroke Scale (NIHSS).We used logistic regression and binomial models to evaluate the associations of $PM_{2.5}$, greenspace, and noise with initial stroke severity adjusting for potential confounders.

Results: Among 2761 patients, higher residential surrounding greenspace was associated with lower risk of severe stroke (OR for NIHSS $>$ 5, 0.75; 95% CI: 0.60–0.95), while, living in areas with higher *Lden* was associated with a higher risk of severe stroke (OR, 1.30; 95% CI: 1.02–1.65). $PM_{2.5}$ was not associated with initial stroke severity.

Conclusions: In an urban setting, surrounding greenspace and traffic noise at home are associated with initial stroke severity, suggesting an important influence of the built environment on the global burden of ischemic stroke.

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[*] Corresponding author. C/ Doctor Aiguader 88, Barcelona, Spain.

[**] Corresponding author. C/ Doctor Aiguader 88, Barcelona, Spain.

E-mail addresses: rvivanco@imim.es (R.M. Vivanco-Hidalgo), cavellaneda@parcdesalutmar.cat (C. Avellaneda-Gómez), payam.dadvand@isglobal.org (P. Dadvand), marta.cirach@isglobal.org (M. Cirach), aois@parcdesalutmar.cat (Á. Ois), 60558@parcdesalutmar.cat (A. Gómez González), 92269@parcdesalutmar.cat (A. Rodriguez-Campello), PDeCeballos@parcdesalutmar.cat (P. de Ceballos), xavier.basagana@isglobal.org (X. Basagaña), anazabalza@gmail.com (A. Zabalza), ecuadrado@parcdesalutmar.cat (E. Cuadrado-Godia), jordi.sunyer@isglobal.org (J. Sunyer), jroquer@parcdesalutmar.cat (J. Roquer), gregory_wellenius@brown.edu (G.A. Wellenius).

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1. Introduction

Ischemic stroke is a leading cause of death and disability in both high-income countries and worldwide (Global et al., 2017), and the overall disability attributable to stroke (102 million disability-adjusted life-years globally in 2010) is expected to increase over the next few decades (Feigin et al., 2010). Therefore, there is a need to improve the understanding of factors related to the burden of stroke.

It is well-established that initial severity of a stroke episode is an important predictor of the level of disability among stroke survivors (Adams et al., 1999). Previous studies have described factors that have been associated with initial ischemic stroke severity, including prevalent classical cardiovascular (CV) risk factors, location of the vascular occlusion, size of the thrombus, and stroke etiology, showing that diabetes and hypertension, central occlusions, thrombus > 5 mm, and cardioembolic etiology predict more severe ischemic strokes (Cuadrado-Godia et al., 2013; Fischer et al., 2005; Hong et al., 2013; Marder et al., 2006).

A number of studies have demonstrated an association between the physical environment near the home and risk of incident stroke. For example, exposure to ambient fine particulate matter (PM) air pollution (PM $< 2.5\,\mu$m in diameter [$PM_{2.5}$]) has been associated with an increased risk of hospitalization for ischemic stroke (Wellenius et al., 2005, 2012; Scheers et al., 2015; Huang et al., 2016). Moreover, environmental noise (especially traffic road noise) has been related to risk of incident cardiovascular events (mainly ischemic heart disease, but also with stroke) (Kempen et al., 2018; Cai et al., 2018). Conversely, living in neighborhoods with more greenspace (i.e., vegetation) has been linked with lower stroke mortality (Wilker et al., 2014; Vienneau et al., 2017).

Interestingly, modifiable characteristics of the social and physical environment have also been associated with initial stroke severity. For example higher socioeconomic status has been linked to lower stroke severity (Rey et al., 2011). Some studies have examined the effect of air pollutants and initial stroke severity, but with contradictory results (Maheswaran et al., 2016a; Wing et al., 2017). We are not aware of any studies considering whether stroke severity is related to either traffic noise or greenspace at the home.

Accordingly, the aim of this study was to assess the association of residential air pollution ($PM_{2.5}$), road traffic noise and surrounding greenspace with initial stroke severity in patients with acute ischemic stroke. We hypothesized that air pollutants and noise would negatively influence initial ischemic stroke severity whereas exposure to greenspace would be associated with less severe strokes.

2. Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

We performed a cross-sectional analysis of the association between residential levels of different environmental factors and initial ischemic stroke severity among patients hospitalized with ischemic stroke. The information regarding environmental and sociodemographic factors was assessed retrospectively at the time of hospital presentation.

2.1. Study design and population

The BASICMAR database (Roquer et al., 2008) is an ongoing prospective register of patients with acute stroke (first episode and recurrence) at University Hospital del Mar, a tertiary public hospital serving an estimated 339,196 residents of two districts (Ciutat Vella and Sant Martí) of the City of Barcelona. Register data are obtained during the index hospital admission from patients, caregivers, relatives, and/or prior medical records. From this database, we identified 2786 patients admitted with an episode of acute ischemic stroke (excluding in-hospital strokes, hemorrhagic strokes, and transient ischemic attacks) between January 1, 2005, and December 31, 2014. All patients included in the register were evaluated by a vascular neurologist, with a complete neurovascular examination including imaging studies and diagnostic tests that confirm the diagnosis of acute ischemic stroke. Demographic data and the following vascular risk factors (based on their presence during the index admission, a prior physician diagnosis or need for medical treatment) were recorded from the BASICMAR database: arterial hypertension (evidence of at least two blood pressure measurements $> 140/90$ mmHg recorded on different days before stroke onset); diabetes (fasting serum glucose level ≥ 7.0 mmol/L); hyperlipidemia (serum cholesterol levels > 220 mg/dL or triglyceride levels > 200 mg/dL); atrial fibrillation (AF) confirmed by an ECG performed during admission, previous ischemic heart disease (IHD), defined as previous history of angina pectoris or myocardial infarction; smoking habit; before stroke onset.

2.2. Environmental and socioeconomic data

Patient addresses were geocoded using information from the Cartographic Institute of Catalonia (ICC). Assessment of spatiotemporal exposure was based on a land use regression (LUR) modeling framework developed in the European Study of Cohorts for Air Pollution Effects (ESCAPE) study (Beelen et al., 2014). Following the ESCAPE protocol, measurement sites for $PM_{2.5}$ were selected. These sites included both traffic and background locations, and represented the gradient of various land use, emission sources, and traffic characteristics. Three 2-week monitoring campaigns were conducted in 2009 during different seasons. Estimates were adjusted using data from an ESCAPE background monitor to account for temporal trends in pollutants between 2009 and the study period (2005–2014) (Cesaroni et al., 2012; Eeftens et al., 2011). GIS (Geographic Information System) data on land uses, traffic indicators, population density, and geographic description of study area were obtained to create potential predictor variables. Multiple linear regression models were constructed following the ESCAPE supervised forward selection protocol using annual average concentrations obtained from the sampling campaign as outcomes. The adjusted R^2 of the final LUR models ranged from 0.71 to 0.85 for the different pollutants, and the cross-validation R^2 ranged from 0.65 to 0.82.

Noise exposure was estimated using Barcelona's municipal strategic noise map (2012) (Tel, 2017). This map follows the recommendations and guidelines of the European Environmental Agency. Exposure to noise (mainly road traffic noise in the study area) was defined as the following four indexes within 50 m and 250 m of each home address: *L*day (from 7 a.m. to 9 p.m.), *L*evening (from 9 p.m. to 11 p.m.), *L*night (from 11 p.m. to 7 a.m.) and *L*den (Day-evening-night-weighted). The *L*day, *L*evening and *L*night indexes are A-weighted sound levels, determined over the corresponding day, evening and night periods. *L*den indicator is an average sound pressure level over all days, evenings and nights in a year. Indexes values (dB) at the street nearest to each participant's residential address were assigned to that participant.

To characterize residential surrounding greenspace, we used the Normalized Difference Vegetation Index (NDVI) derived from the Landsat 8 Operational Land Imager (OLI) sensor data at 30 m × 30 m resolution. Given that the maximum vegetation in our study region occurs in the spring and autumn months, the Landsat image from April 16, 2013 was selected in order to maximize the contrast in exposure (Dadvand et al., 2012). The findings of our previous studies support the stability of the NDVI spatial contrast over years in the study region (Dadvand et al., 2012). Usually, areas of barren rock, sand, or snow

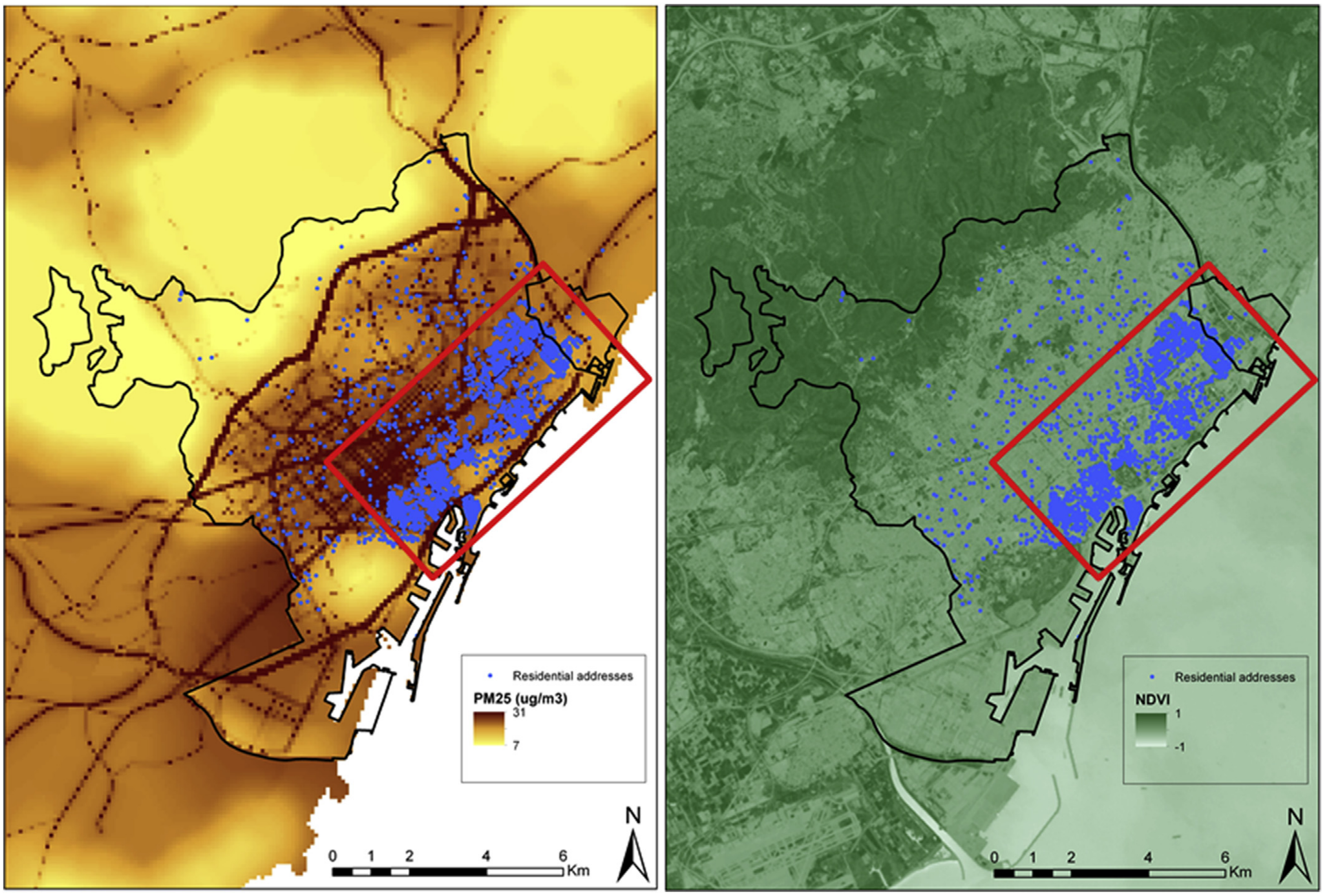

Fig. 1. Map of the city of Barcelona. The red square outlines the two districts assessed. Blue dots represent patients. Intensity of brown color depicts $PM_{2.5}$ concentration (corresponding to the standard road map) and the intensity of green color, NDVI concentration. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

usually show very low NDVI values (< 0.1) and sparse vegetation such as grasslands result in moderate NDVI values (0.2–0.5). Residential surrounding greenspace was quantified as the average NDVI within 100, 300, and 500 m around each participant's residential geocoded address.

Fig. 1 represents a map of the city of Barcelona where intensity of brown color depicts $PM_{2.5}$ concentration (corresponding to the standard road map) and the intensity of green color, NDVI concentration.

Urban Vulnerability Index is a measure of neighborhood socioeconomic status (NSS) at the census tract level (median area of 0.08 km^2 for the study area) based on 21 indicators of urban vulnerability grouped into four themes: sociodemographic vulnerability (five indicators), socioeconomic vulnerability (six indicators), housing vulnerability (five indicators), and subjective perception of vulnerability (five indicators) (Atlas of urban vulnerabil, 2012). This measure of NSS has been widely used in previous studies and has showed strong correlations with individual socioeconomic status indicators such as “temporary employment”, “unskilled work” and “illiteracy” (Bosch de Basea et al., 2018; Valentin et al., 2018).

2.3. Stroke severity outcome

The primary outcome for this analysis was initial stroke severity measured by the National Institute of Health Stroke Scale (NIHSS; 0–42) score, considering the higher the score, the greater the stroke severity. The NIHSS is a 15-item neurologic examination stroke scale used to evaluate the effect of stroke on the levels of consciousness, language, neglect, visual-field loss, extraocular movement, motor strength, ataxia, dysarthria, and sensory loss. A trained observer rates the patent's ability to answer questions and perform activities. Ratings for each item are scored with 3–5 grades with 0 as normal, and there is an allowance for untestable items (see Supplementary material). Moderate to severe stroke was defined as NIHSS score > 5 based on previous studies (Adams et al., 1999; Khatri et al., 2015; Sandercock et al., 2012). The NIHSS score was assessed by the neurologist in charge once the patient arrived at the emergency room and every score was recorded from the BASICMAR database.

2.4. Statistical analysis

We performed a descriptive analysis of the sociodemographic and clinical variables calculating percentages for categorical variables and mean with corresponding standard deviations (or median with interquartile range in case of not normally distributed) for quantitative variables.

We considered all the environmental exposure variables (air pollutant concentration $PM_{2.5}$, every noise indicator- *Lday, Levening, Lnight and Lden*- and average NDVI for 100, 300 and 500 m) modeled as quartiles for the main analysis. Analysis considering all the exposure variables modeled as linear continuous (interquartile range increments) were also performed.

We used logistic and negative binomial regression models to evaluate the association between $PM_{2.5,}$ traffic noise, greenspace and severity (considered either as dichotomously NIHSS score > 5 and as continuous variable). We modeled each association for each environmental factor as follows: a) Model 1, adjusted for age, sex, smoking, and

NSS; b) Model 2, Model 1 plus cardiovascular risk factors and previous history of coronary heart disease or stroke; c) Model 3, a multi-environmental model ($PM_{2.5}$, road traffic noise and greenspace), adjusted for the rest of covariables (age, sex, smoking, NSS, cardiovascular risk factors, previous history of coronary heart disease or stroke). Noise indicators were considered individually in each model (i.ea separate model for each noise indicator). Models were not adjusted for stroke etiology as etiology is potentially a causal mediator between environmental factors and stroke severity.

Regarding greenspace models, the main analysis was done using NDVI buffer within 300 m; sensitivity analyses were also performed using NDVI buffer within 100 and 500 m.

2.5. Ethical consideration

The information used in this study was collected from the prospective BASICMAR register, with the approval of our local ethics committee. All patients (or their proxies) provided informed consent prior to their inclusion in the study registry.

3. Results

3.1. Clinical and environmental characteristics

Of the 2786 patients hospitalized with acute ischemic stroke from the Ciutat Vella and Sant Martí district and included in the BASICMAR register during the study period, 25 were excluded due to admission date errors or unknown (9 patients) or missing initial NIHSS (16 patients). The final sample included 2761 patients with ischemic stroke. Sociodemographic, clinical and environmental characteristics are described in Table 1.

The majority of the patients lived in moderately disadvantaged neighborhoods. Hypertension was the most frequent cardiovascular risk factor (76.5%). There was only a high correlation across noise indicators, not between any other exposures metric (Table 2).

Table 1
Sociodemographic characteristics of patients with acute ischemic stroke (n = 2761).

Sociodemographic characteristics	Mean (SD) or Median [IQR] or n (%)
Age, y	75 (12.5)
Female	1399 (50.7)
Neighborhood Socioeconomic Status[a]	0.68 (0.20)
Cardiovascular risk factors and comorbidities	
Current smoker	568 (20.6)
Hypertension	2111 (76.5)
Diabetes Mellitus	958 (34.7)
Dyslipidemia	1239 (44.9)
Previous history of coronary heart disease	429 (15.5)
Previous history of stroke	550
Atrial Fibrillation	719
Outcome	
NIHSS	5 [3–12]
NIHSS > 5	1267 (45.9)
Environmental characteristics	Mean (SD) or Median [IQR]
$PM_{2.5}$ (μg/m^3)	17.89 [15.20–21.88]
NDVI average**	
100 m	0.154 [0.125–0.199]
300 m	0.166 [0.136–0.204]
500 m	0.170 [0.138–0.200]
Road traffic noise level at nearest street (dB)	
LDay	63 (4.9)
LEvening	61 (4.9)
LNight	55 (5.5)
Lden	65

[a] NSS index where 1 more deprived and 0 less deprived. **NDVI average within 100, 300 and 500 m buffer where 1 is most greener and 0, less.

Table 2
Spearman correlation matrix between all pairs of the exposures. All correlations were statistically significant. PM2.5: particulate matter 2.5 μm; NDVI 300: Normalized Difference Vegetation Index within 300 m; Lday:day noise indicator; Levening: evening noise indicator; Lnight: night noise indicator; Lden: average noise indicator.

	$PM_{2.5}$	NDVI300	*Lday*	*Levening*	*Lnight*
$PM_{2.5}$	1				
NDVI300	−0.12	1			
Lday	0.24	−0.08	1		
Levening	0.24	−0.18	0.94	1	
Lnight	0.25	−0.15	0.92	0.94	1
Lden	0.25	−0.13	0.97	0.96	0.98

3.2. Associationof environmental factors on initial stroke severity

Higher residential surrounding greenspace (4th quartile compared to 1st quartile) in 300 m buffer was associated with less severe acute ischemic stroke (OR of NIHSS > 5, 0.75; 95% CI 0.60–0.95). Conversely, living in areas with higher average noise (*Lden*, 4th quartile compared to 1st quartile) had a higher risk of severe stroke (OR, 1.30; 95% CI: 1.02–1.65). Residential $PM_{2.5}$ was not associated with initial stroke severity (see Tables 3 and 4).When adjusting for $PM_{2.5}$ levels and *Lden*, the protective effect of greenspace persisted (Table 5).

Sensitivity analyses considering NDVI within 500 m buffer were consistent with those of the main analysis. Results considering NDVI within a 100 m buffer were in the same direction, but not statistically significance (see Appendices TableA1 and Table A2a and A2b). Results considering environmental exposure variables modeled as linear continuous variables (IQR increments) were similar to the main analysis

Table 3
Odds ratio (OR) and 95% confidence interval of being hospitalized with a severe ischemic stroke defined as an initial NIH Stroke Scale score of > 5. $PM_{2.5}$, noise indicators and residential surrounding greenspace at 300 m, all modeled as quartiles variables, with Q1 being the lowest concentration/value and taken as reference. Stroke severity modeled as dichotomous variable NIHSS > 5.Model 1: adjusted by age sex, smoking status and NSS; Model 2: model 1 plus hypertension, diabetes mellitus, dyslipidemia, prior history of coronary heart disease, prior history of stroke/transient ischemic attack. Test of linear trend across quartiles: PM2.5 p = 0.469; *LDay* p = 0.053 *LEvening* p = 0.016 *LNight* p = 0.068 *Lden* p = 0.027 NDVI_300 p = 0.010.

Exposure	Stroke severity (NIHSS > 5) OR (95% CI)	
	Model 1	Model 2
Annual $PM_{2.5}$		
Q2	1.03 (0.82–1.30)	1.01 (0.80–1.26)
Q3	1.00 (0.80–1.23)	0.93 (0.74–1.17)
Q4	1.10 (0.88–1.40)	1.04 (0.83–1.31)
LDay		
Q2	1.11 (0.90–1.40)	1.10 (0.88–1.37)
Q3	1.10 (0.90–1.35)	1.10 (0.88–1.35)
Q4	**1.31 (1.01–1.70)**	1.30 (0.99–1.67)
LEvening		
Q2	1.02 (0.82–1.30)	1.00 (0.80–1.36)
Q3	1.16 (0.93–1.44)	1.14 (0.91–1.42)
Q4	**1.30 (1.04–1.63)**	**1.27 (1.01–1.60)**
LNight		
Q2	1.04 (0.83–1.30)	1.04 (0.83–1.31)
Q3	1.14 (0.91–1.41)	1.12 (0.90–1.4)
Q4	1.23 (1.00–1.54)	1.23 (0.98–1.55)
Lden		
Q2	1.05 (0.85–1.30)	1.05 (0.85–1.3)
Q3	1.15 (0.91–1.46)	1.15 (0.90–1.46)
Q4	**1.30 (1.03–1.65)**	**1.30 (1.02–1.65)**
NDVI 300 m		
Q2	1.01 (0.80–1.26)	1.03 (0.81–1.30)
Q3	**0.70 (0.56–0.88)**	**0.71 (0.60–0.90)**
Q4	**0.76 (0.60–0.95)**	**0.75 (0.60–0.95)**

Table 4
Association between environmental factors and initial NIH Stroke Scale score as a continuous variable using negative binomial regression. $PM_{2.5}$, noise indicators and residential surrounding greenspace at 300 m, all modeled as quartiles variables, with Q1 being the lowest concentration/value and taken as reference. Stroke severity modeled as continuous. Model 1: adjusted by age sex, smoking status and NSS; Model 2: model 1 plus hypertension, diabetes mellitus, dyslipidemia, prior history of coronary heart disease, prior history of stroke/transient ischemic attack. Test of linear trend across quartiles: PM2.5 p = 0.286; *LDay* p = 0.018 *LEvening* p = 0.017 *LNight* p = 0.069 *Lden* p = 0.025 NDVI_300 p = 0.015.

Exposure	Stroke severity (NIHSS) B Coefficient (95% CI)	
	Model 1	Model 2
Air pollutant concentration		
Annual $PM_{2.5}$		
Q2	−0.14 (−0.11-0.08)	−0.01 (-0.10-0.08)
Q3	0.02 (−0.07-0.11)	0.00 (-0.09-0.97)
Q4	0.12 (−0.08-0.11)	0.00 (-0.09-0.09)
Road traffic noise		
LDay		
Q2	0.066 (−0.02-0.16)	0.06 (−0.02-0.15)
Q3	**0.09 (0.00–0.18)**	**0.09 (0.00–0.18)**
Q4	0.09-(-0.016-0.20)	0.08 (−0.02-0.19)
LEvening		
Q2	0.03 (−0.06-0.13)	0.03 (−0.06-0.13)
Q3	**0.09 (0.00–0.18)**	0.09 (−0.00-0.18)
Q4	0.08 (−0.01-0.18)	0.07 (−0.01-0.17)
LNight		
Q2	0.04 (−0.05-0.13)	0.04 (−0.05-0.13)
Q3	0.08 (−0.01-0.17)	0.07 (−0.02-0.16)
Q4	0.08 (−0.01 (0.17)	0.08 (−0.01-0.17)
Lden		
Q2	0.05 (−0.04-0.14)	0.05 (−0.04 -0.14)
Q3	0.09 (−0.01-0.19)	0.08 (−0.01-0.18)
Q4	0.09 (−0.00-0.19)	0.09 (−0.01-0.19)
Residential surrounding greenspace		
NDVI 300 m		
Q2	0.01 (−0.08-0.10)	−0.01 (−0.08-0.11)
Q3	−0.08 (−0.18-0.01)	−0.08 (−0.17-0.015)
Q4	**−0.09 (-0.19–-0.00)**	**−0.11 (-0.21- - 0.01)**

Table 5
Results of logistic and binomial regression multienvironmental model of the association between exposure to environmental factors and stroke severity. $PM_{2.5}$, *Lden* indicator and residential surrounding greenspace at 300 m, all modeled as quartiles variables, with Q1 being the lowest concentration/value and taken as reference. Stroke severity modeled either as dichotomous NIHSS > 5 as continuous.Model 3: model 2 plus all environmental exposures ($PM_{2.5}$, *Lden* and NDVI 300 m).

Exposure	Model 3	
	Dichotomous NIHSS > 5 OR (95% CI)	Change in NIHSS (95% CI)
Air pollutant concentration		
Annual $PM_{2.5}$		
Q2	0.97 (0.77–1.21)	−0.03 (−0.13-0.06)
Q3	0.88 (0.7–1.11)	−0.02 (−0.11-0.07)
Q4	0.95 (0.75–1.20)	−0.03 (−0.13-0.06)
Road traffic noise		
Lden		
Q2	1.04 (0.84–1.30)	0.05 (−0.04-0.14)
Q3	1.16 (0.91–1.48)	0.09 (−0.01-0.19)
Q4	1.19 (0.93–1.53)	0.06 (−0.13-0.06)
Residential surrounding greenspace		
NDVI 300 m		
Q2	1.00 (0.79–1.27)	0.01 (−0.09-0.10)
Q3	**0.71 (0.56–0.90)**	−0.08 (−0.18-0.01)
Q4	**0.76 (0.60–0.95)**	**−0.11 (-0.21–0.014)**

(see Appendices Table A3 and Table A4a and A4b).

4. Discussion

To our knowledge, this is the first study simultaneously evaluating the influence of an array of urban-related exposures on initial stroke severity which also adds to the scarce available evidence on environmental determinants of this health endpoint. The individuals studied were part of a clinically well-described sample of patients with acute ischemic stroke, which facilitated to adjust for different factors (age, CV risk factors and NSS) that have been previously described to be related with severity. We observed that higher residential surrounding greenspace had a potential beneficial influence on initial stroke severity. This association persisted after adjusting for other environmental factors ($PM_{2.5}$ and noise) in multi-exposure models. Exposure to noise was associated with more severe initial stroke, however, the association did not persist after adjustment for other environmental factors ($PM_{2.5}$ and greenspace). For air pollution our findings were not conclusive.

There is growing evidence supporting the beneficial health influences exposure to greenspace. This exposure has been associated with improved mental and physical health, including lower risk of mortality and morbidity (Kondo et al., 2018).For instance, higher residential surrounding greenspace has been associated with lower risk of cardiovascular mortality (Gascon et al., 2016) and clinical visits for cardiovascular problems (Maas et al., 2008); however, there are inconsistencies in these reported associations (Tamosiunas et al., 2014).

Residential proximity greenspace has been shown to be related with lower stroke admissions (Foster et al., 2012) and with higher survival rates after acute ischemic stroke (Wilker et al., 2014; Vienneau et al., 2017). However, the available evidence on the association between this exposure and stroke is still very scarce, with no study reporting on the association with severity of stroke.

Different mechanisms have been hypothesized for how exposure to greenspace might have a beneficial effect on health. On one hand, it might promote stress reduction (Triguero-Mas et al., 2017), social interactions (Maas et al., 2009) and physical activity (Maas et al., 2008). In fact, a recent study found an association between prestroke regular physical activity and initial stroke severity (Reinholdsson et al., 2018). On the other, exposure to greenspace has been associated with an immunoregulatory effect (Rook, 2013), lower levels of sympathetic activation, reduce oxidative stress, and higher angiogenic capacity (Yeager et al., 2018). These mechanisms could potentially be implicated in the initial formation of the thrombus and the systemic inflammatory response to stroke, and thus, initial severity. However, there is a need for further research in this area to understand the possible mechanisms by which prestroke exposure to greenspace would influence stroke severity.

In this study we also observed that patients living in areas with higher annual average noise values had a 20% higher risk of severe stroke, compare to those living in areas with lower average noise values. This association did not persist after adjustment for NDVI and air pollution.

Road traffic noise has also been related with adverse CV outcomes (Cai et al., 2018), but few studies have assessed the influence on stroke, suggesting that traffic noise might play a deleterious role increasing its risk (Halonen et al., 2015). There are no studies, though, testing specifically its effect in acute ischemic stroke severity. A possible mechanism that could explain the association is that noise may also lead to endothelial dysfunction and arterial hypertension (Munzel et al., 2018).

Air pollution has been related with higher risk of acute ischemic stroke events (Wang et al., 2014; Vivanco-Hidalgo et al., 2018) and higher mortality (Scheers et al., 2015). We did not find any association between exposure to long-term air pollutant concentrations ($PM_{2.5}$) and stroke severity. There are few studies that have tested the effect on severity and results are contradictory (Wing et al., 2017; Andersen et al., 2010). Our results were in line with a previously study performed in a similar cohort in another urban setting (London) that showed no association between air pollution exposure and stroke severity (Maheswaran et al., 2016b).

Our study had several limitations. The urban environment across the two districts of Barcelona where patients lived offered limited variability in exposure to environmental factors (Fig. 1). On the other hand, despite the different timeframes from which we obtained the data from noise map indicators, satellite-based NDVI values and spatial estimates of air pollutant levels generated by land-use regression models, we effectively assumed that the city spatial surface and the spatial distribution of (road traffic) noise, greenspaces and air pollutants remained constant over the study period. There are some reports supporting the stability of the spatial contrasts for noise (Dadvand et al., 2014a), greenspace (Nieuwenhuijsen et al., 2018; Dadvand et al., 2014b) and air pollution (Cesaroni et al., 2012; Eeftens et al., 2011) in the study region. Furthermore, to our knowledge, there was no major change in land use, emissions profiles, or traffic flow between the year of land-use regression model construction (2009) and the years of our study (2005–2014).

Our use of satellite-based NDVI to assess greenspace surrounding participants' homes enabled us to take account of small-area green spaces (e.g. roadside trees and home gardens) in a standardized way; however, NDVI does not distinguish between different types of vegetation (e.g. trees, shrubs, grasses, etc.) which could have been relevant in our evaluated association. NDVI measures do not take the quality or frequency of use of green spaces into account. Quality characteristics of green spaces like aesthetics, biodiversity, walkability, sport/play facilities, safety, and organized social events have been suggested to predict the use of green spaces (McCormack et al., 2010) and could have an effect on our investigated associations.

We did not have data regarding individual socioeconomic status. This factor might have influence in patients' lifestyle behavior (and, for example, individuals with higher socioeconomic status might be prone to live nearby more dense green areas). However, the adjustment for a robust index of area vulnerability (including 21 items) and a set of comorbidities strongly related to social class might have reduced the likelihood for a potential residual confounding for social class.

We have considered as initial severity the first NIHSS score assessed once the patient arrived at the emergency room. It is known that ischemic stroke is an acute disease and its severity is mainly established at the very beginning of the episode and driven by the location and characteristic of the arterial thrombus. However, it is possible that some stroke patients could initially present with fluctuating symptoms and that other factors such as distance to the hospital, living conditions, or the presence of a bystander could have influence the initial score assessment of the stroke severity.

5. Conclusion

Our study found that, in an urban setting, residential surrounding greenspace and traffic noise were associated with initial stroke severity, suggesting an important influence of the built environment on the global burden of stroke. Further studies are needed to assess which aspects of exposure to neighborhood green spaces could influence the initial severity of ischemic stroke.

Disclosures

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2019.108725.

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